

QUARTERLY FOCUS ISSUE: HEART FAILURE**State-of-the-Art Paper**

Palliative Care in Congestive Heart Failure

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Symptoms and compromised quality of life prevail throughout the course of heart failure (HF) and thus should be specifically addressed with palliative measures. Palliative care for HF should be integrated into comprehensive HF care, just as evidence-based HF care should be included in end-of-life care for HF patients. The neurohormonal and catabolic derangements in HF are at the base of HF symptoms. A complex set of abnormalities can be addressed with a variety of interventions, including evidence-based HF care, specific exercise, opioids, treatment of sleep-disordered breathing, and interventions to address patient and family perceptions of control over their illness. Both potential sudden cardiac death and generally shortened length of life by HF should be acknowledged and planned for. Strategies to negotiate communication about prognosis with HF patients and their families can be integrated into care. Additional evidence is needed to direct care at the end of life, including use of HF medications, and to define management of multiple sources of distress for HF patients and their families. (J Am Coll Cardiol 2009;54:386–96) © 2009 by the American College of Cardiology Foundation

Heart failure (HF) is an increasingly prevalent clinical syndrome that limits length of life and profoundly impacts function and quality of life. Recent epidemiologic analysis demonstrates increasing incidence and improved survival of persons with HF, resulting in a growing population of individuals living with HF, who by definition are symptomatic. Heart failure is responsible for significant health care system and individual burden. As therapies for HF improve survival, growing numbers of HF patients live with this burden; many have advanced HF, and large numbers, by virtue of being old, have comorbid conditions or are frail.

Although the discipline of palliative care began with a focus almost exclusively on end-of-life care, it was reconceptualized as recognition grew of the multiple domains of distress patients with life-limiting illnesses and their families experience throughout the course of illness. Significant symptoms and psychosocial distress begin during treatments intending to extend life or to cure potentially life-limiting illness. The World Health Organization modified its definition in 2002 to state that palliative care should be provided “early in the course of illness, in conjunction with other therapies that are intended to prolong life” (1). Palliative care includes multiple disciplines to address distress from symptoms and other aspects of the illness in the patient and in the family who are treated as a unit, as the well-being of one impacts the other (2). Communication with the patient and family and patient-centered decision making are integral to palliative care. Consensus panels and guidelines

advocated provision of palliative or supportive care concurrent with efforts to prolong life in HF (3), and at the end of life (4,5).

This paper will review the current understanding of symptom etiology and palliation in HF, and practical aspects of communication and end-of-life care.

Comprehensive HF Care

Patients with HF generally are symptomatic for some time before presenting for evaluation and receiving the diagnosis of HF. With initiation of appropriate medications, diet and fluid management, and other interventions, the symptom burden may diminish, but for many patients, exertion remains limited, general fatigue persists, and social structures, including work and interpersonal relationships, are altered.

Palliative or supportive care to address symptom, psychosocial, or existential distress and strategies to manage and cope with HF should be provided concurrently with evidence-based disease-modifying interventions in comprehensive HF care. Figure 1 and Table 1 depict a scheme for conceptualizing comprehensive HF care. Early in HF therapy, supportive efforts focus on education for the patient and family about HF and self-management. Diuresis and evidence-based therapies achieve a plateau of improved function. Even when a plateau of improved function is achieved, the patient and family will benefit from efforts that improve symptoms and assist the patient and family in coping with their HF and its impact on their lives. Heart transplantation or destination therapy ventricular assist devices improve function for patients for a period and carry a different burden of chronic illness. At the end of life or

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when significant physical frailty or comorbidities predominate, the major focus of care is palliation, but some HF therapies remain important. Heart failure differs from cancer in which potentially curative treatments are discontinued as the patient reaches the end stage.

Communication and decision making between clinicians and patients about therapies and devices must also be integrated into comprehensive HF care. Education and discussions ideally occur over time linked to what the patient values, and may require refreshing or revision at turning points in the patient’s course.

Who should provide palliative care? Primary care clinicians provide the majority of HF care, thus they must ally with expert HF and palliative care clinicians to provide comprehensive HF care. All cardiologists and HF specialists should align with other disciplines to provide comprehensive HF care.

In large centers, palliative care might be provided by a specific interdisciplinary team that focuses on relief of suffering (physical, psychosocial, and spiritual) distinct from and in addition to HF care. In general, however, creating a dichotomy with palliative care as a supplement to life-prolonging management is inappropriate to HF (6). Rather, comprehensive management of HF should integrate palliative or supportive care with the evidence-based medications, devices, and surgeries that intend to address HF pathophysiology, precisely because the physical and psychiatric distress and social issues are intertwined with HF pathophysiology. Therapies addressing HF pathophysiology that improve survival and cardiac function simultaneously palliate HF-related symptoms.

Etiology of symptoms in HF. Heart failure patients experience symptoms of fatigue and lack of energy, dyspnea,

depression, pain, and cognitive impairment, among other problems (7). The etiology of HF symptoms is complex and incompletely understood. Although most patients have worsened dyspnea with episodes of volume overload, HF-related dyspnea and exertional fatigue are not directly related to pulmonary capillary wedge pressure or cardiac output, rather to broader, systemic effects of HF, including generalized myopathy (8). Some symptoms may overlap with comorbid problems, which are particularly prevalent in older individuals with HF (9). Symptoms reported by HF patients are significantly impacted by depression and by the patients’ perceived control over their condition (10).

Symptoms have been studied primarily in HF due to left ventricular systolic dysfunction (LVSD). Similar pathologic abnormalities in inflammatory and neuroendocrine function are seen in heart failure with normal ejection fraction (HFnEF, also called “preserved systolic function” and “diastolic dysfunction”).

Figure 2 schematically presents the pathophysiologic changes of HF and their relation to symptoms. Regardless of etiology, HF is characterized by alterations in the renin-angiotensin-aldosterone, sympathetic, and other hormonal systems, resulting in a catabolic state (11). Proinflammatory cytokines are activated in HF, leading to insulin

Abbreviations and Acronyms
CPAP = continuous positive airway pressure
ESAS = Edmonton Symptom Assessment System
HF = heart failure
HFnEF = heart failure with normal ejection fraction
LVSD = left ventricular systolic dysfunction
NYHA = New York Heart Association
SCD = sudden cardiac death
SSRI = selective serotonin reuptake inhibitor

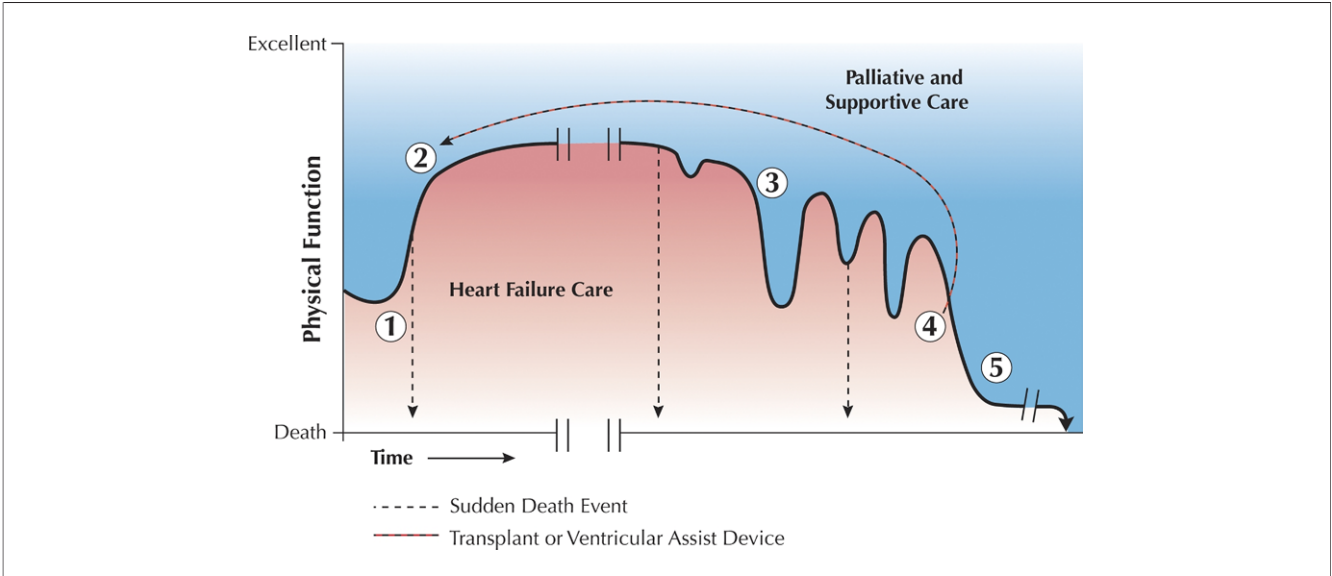


Figure 1 Schematic Depiction of Comprehensive Heart Failure Care

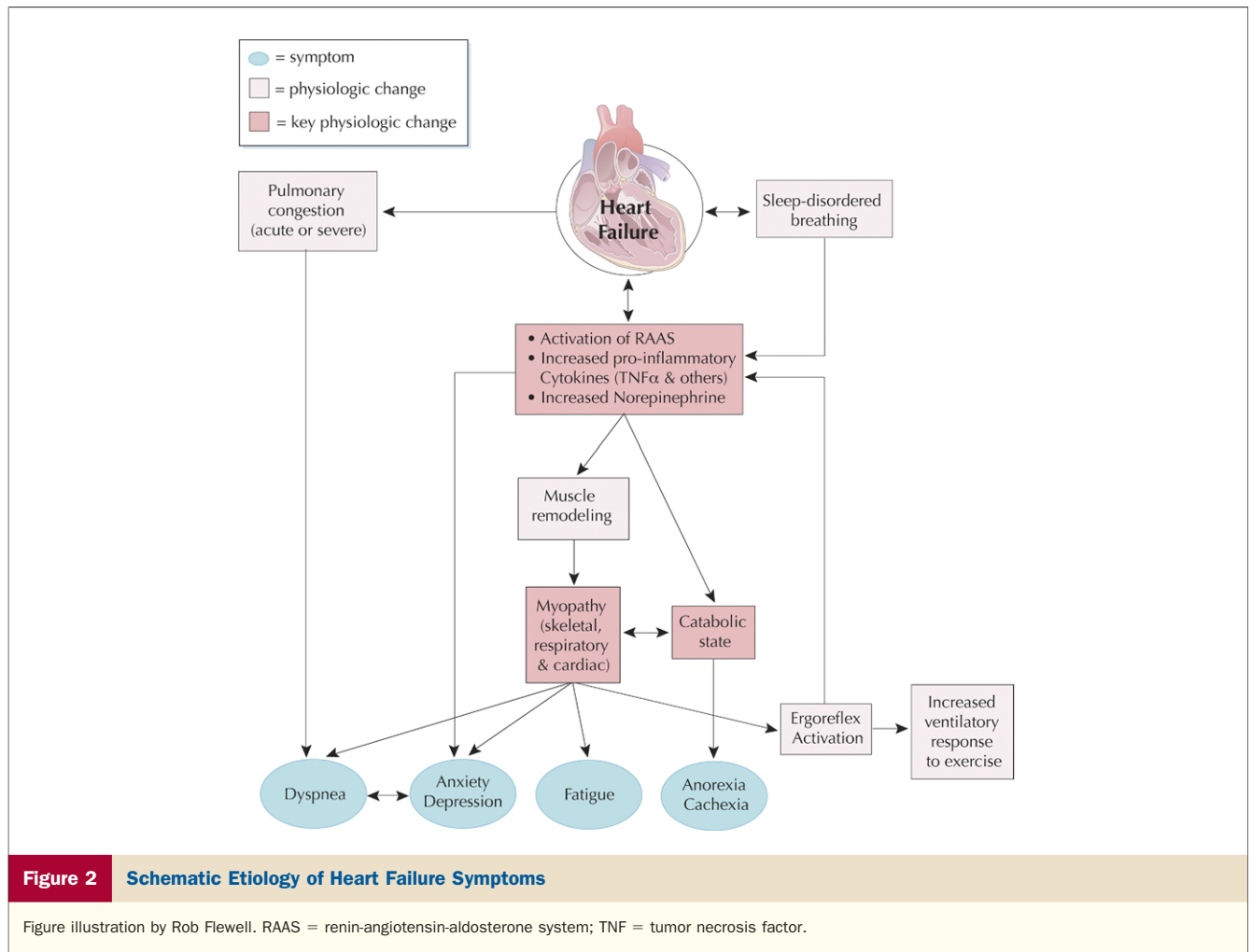
Figure illustration by Rob Flewell.

Table 1 Comprehensive HF Care

	Phase 1	Phase 2	Phase 3	Phase 4	Phase 5
	Initial symptoms of HF develop and HF treatment is initiated	Plateau of variable length reached with initial medical management, or following mechanical support or heart transplant	Functional status declines with variable slope; intermittent exacerbations of HF that respond to rescue efforts	Stage D HF, with refractory symptoms and limited function	End of life
NYHA functional classification	II–III	II–IV	III ^B	IV	IV
HF care and interventions	<ul style="list-style-type: none"> Identify etiology of HF Eliminate precipitating factors and causative conditions Diuretics→euvoolemia ACE inhibitor Beta-blocker Evaluate for coexistent conditions¹ 	<ul style="list-style-type: none"> Spironolactone if NYHA functional class III–IV Digoxin if NYHA functional class III–IV and LVEF <35% Hydralazine/nitrates? Evaluate and treat for sleep-disordered breathing ICD if EF <35% and defibrillation desired for SCD CRT or CRT/D? 	<ul style="list-style-type: none"> Re-evaluate medication and compliance Re-evaluate for precipitating factors, and coexistent conditions Diuretics→euvoolemia 	<ul style="list-style-type: none"> Evaluate for heart transplant Evaluate for destination LVAD Meticulous fluid management Inotrope trial if hypotensive and volume-overloaded (LVSD) Intravenous nitrates/hydralazine? 	<ul style="list-style-type: none"> Discontinue medications not impacting symptoms Continue ACE inhibitor or ARB, titrate beta-blocker dose, or stop if hypotensive Diuretics→euvoolemia Inotrope trial if hypotensive and volume-overloaded
Decision-making	<ul style="list-style-type: none"> Preferences for CPR/defibrillator Durable power of attorney for health care or proxy 	<ul style="list-style-type: none"> Defibrillator for primary prevention of SCD? Durable power of attorney for health care or proxy decision-maker General goals for care, preferences for unacceptable health states 	<ul style="list-style-type: none"> Urgent care decisions using doctor's best judgment or clear patient preferences Are advanced or invasive therapies indicated? Are advanced therapies consistent with patient preferences? 	<ul style="list-style-type: none"> Candidate for transplant or destination VAD? Is palliative care appropriate? Does patient benefit from inotrope infusion? Review preferences for CPR/defibrillator 	<ul style="list-style-type: none"> Clarify goals of care Site of care (hospital, home, other) Health care delivery (hospice, other provider) How to manage death (review CPR decision, review ICD and other devices; if appropriate, plan deactivation)
Supportive care					
A. Communication	<ul style="list-style-type: none"> Understand patient concerns and fears Identify life-limiting nature of HF Elicit preferences for care in emergencies or sudden death and for information and role in decision-making Elicit symptoms and assess QOL 	<ul style="list-style-type: none"> Elicit symptoms and assess QOL Re-evaluate resuscitation preferences for care in emergencies Set goals for care Identify coping strategies Re-educate about sodium, weight, and volume status 	<ul style="list-style-type: none"> Elicit symptoms and QOL Elicit values and re-evaluate preferences Identify present status and likely course(s) Re-evaluate goals of care Re-educate about sodium, weight, and volume status, medication compliance 	<ul style="list-style-type: none"> Elicit symptoms Acknowledge present status Elicit preferences and reset goals of care Identify worries Review appropriate care options and likely course with each Explore suitability and preferences about surgery or devices 	<ul style="list-style-type: none"> Elicit desired symptom relief and identify medication for symptom goals Assistance with delivery of care Preferences for end-of-life care, site of care, family needs, and capabilities Plan after death (care of the body, notifications, memorials, burial)
B. Education	<ul style="list-style-type: none"> Patient and family self-management (sodium, weight and volume) Diet, exercise HF course including sudden death and options for management 	<ul style="list-style-type: none"> What to do in an emergency Review self-management 	<ul style="list-style-type: none"> Review self-management Review what to do in an emergency Symptom management Eliminate NSAIDs 	<ul style="list-style-type: none"> Optimal management for given care approach Interventions for deterioration in status What to do in an emergency 	<ul style="list-style-type: none"> Likely course and plans for management of events Symptom management What to do for worsened or change in status What to do when death is near and at the time of death
C. Psychosocial and spiritual issues	<ul style="list-style-type: none"> Coping with illness Insurance and financial resources Insurance and financial resources regarding medications and loss of income Emotional and spiritual support 	<ul style="list-style-type: none"> Roles and coping for patient and family Emotional support Spiritual support Social interaction Evaluate both patient and family anxiety, distress, depression, impaired cognition 	<ul style="list-style-type: none"> Family stresses and resources Re-evaluate patient and family needs Caregiver education and assistance with care Evaluate cognition and initiate compensation 	<ul style="list-style-type: none"> Insurance coverage Re-evaluate stresses, needs, and support patient and family Address spiritual and existential needs Support coping with dying 	<p>For both patient and family:</p> <ul style="list-style-type: none"> Address anxiety, distress, depression Address spiritual and existential needs, concerns regarding dying Anticipatory grief support Assist in care provision Post-death bereavement
D. Symptom management	<ul style="list-style-type: none"> HF medications for dyspnea Exercise/endurance training for fatigue Antidepressant for depression (check Na⁺ with SSRIs) Local treatment and/or opioids for pain 	<ul style="list-style-type: none"> Identify new or worsened symptoms CPAP/O₂ for sleep-disordered breathing for fatigue Exercise program (lower extremity strengthening) Local treatment and/or opioids for pain SSRI or tricyclic or stimulant for depression 	<ul style="list-style-type: none"> Oxygen for dyspnea; consider opioids for acute relief of dyspnea Lower extremity strengthening for dyspnea/fatigue CPAP/O₂ for sleep-disordered breathing Local treatment and/or opioids for pain Benzodiazepines/counseling for anxiety Stimulant for depression 	<ul style="list-style-type: none"> Oxygen for dyspnea Opioids for dyspnea Lower extremity and inspiratory strengthening CPAP/O₂ for sleep-disordered breathing Local treatment and/or opioids for pain Benzodiazepines/counseling for anxiety Stimulant for depression 	<ul style="list-style-type: none"> Opioids for dyspnea and pain Oxygen for dyspnea Stimulants for fatigue Benzodiazepines/ counseling for anxiety Lower extremity strengthening for fatigue and dyspnea CPAP/O₂ for sleep-disordered breathing Stimulant for depression

¹Coexistent conditions: atrial fibrillation with uncontrolled rate, sleep-disordered breathing, anemia, physical frailty, coexistent pulmonary disease.

ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; CPAP = continuous positive airway pressure; CPR = cardiopulmonary resuscitation; CRT = cardiac resynchronization therapy; CRT/D = cardiac resynchronization therapy defibrillator; EF = ejection fraction; HF = heart failure; ICD = implantable cardioverter-defibrillator; LVAD = left ventricular assist device; LVEF = left ventricular ejection fraction; LVSD = left ventricular systolic dysfunction; NSAID = nonsteroidal anti-inflammatory drug; NYHA = New York Heart Association; QOL = quality of life; SCD = sudden cardiac death; SSRI = selective serotonin reuptake inhibitor; VAD = ventricular assist device.



resistance, cachexia, and anorexia, and contributing to the catabolic state (12). These hormonal and cytokine alterations result in respiratory and skeletal muscle atrophy and weakness, which contribute to symptoms of fatigue, dyspnea, and limited exercise capacity. The muscle abnormalities in HF are quite similar to “sarcopenia” of aging (13), which also likely relates to abnormalities of the renin-angiotensin-aldosterone system (14), and proinflammatory abnormalities common in the aged. Because the vast majority of HF patients are elderly, there is significant overlap between HF and other prevalent conditions in aging. The underlying neurohormonal and cytokine derangement, myopathy and other abnormalities have been well-described in young HF patients and therefore play a significant role in the pathophysiology of HF symptoms.

Heart failure patients have increased ventilatory rates for a given volume of expired carbon dioxide (V_E/V_{CO_2}) that cause tachypnea for a given work load, but are independent of symptomatic dyspnea. Dyspnea (the perception of difficulty breathing) may not be subjectively present in HF patients despite increased respiratory rate. The ergoreflex in muscle (in response to work, ergoreceptors stimulate ventilation and activate sympathetic hormones) impact ventila-

tory effort as do central and pulmonary chemoreceptors (which respond to carbon dioxide) and pulmonary J receptors (that likely respond to congestion or alveolar stiffness). Overt pulmonary edema is associated with dyspnea, and its relief with improvement in dyspnea, although left ventricular function or volume status per se do not relate specifically to exercise capacity, fatigue, or dyspnea (15).

Sleep-disordered breathing, which is present in approximately one-half of HF patients, complicates HF management and contributes to daytime fatigue. Oxygen desaturation causes marked elevations in norepinephrine that in turn contribute to anxiety and depression, as well as worsen sympathetic derangement. Cognitive impairment is prevalent in HF. Impaired memory and executive function, the ability to relate and sequence information, cause difficulty recognizing worsened HF status and complying with the complex medication regimen for HF. Comorbid obesity, pulmonary disease, or frailty may also contribute to the symptom spectrum in HF.

Assessment of symptoms. The New York Heart Association (NYHA) level has been used as a proxy for symptom assessment in HF; however, this scale is a general statement by the clinician reflecting physical function and symptom

severity. Physician and patient report of NYHA status do not correlate well (16), and NYHA also differs from a classification based on metabolic equivalents assigned to patient-reported activity (17). Tools to assess symptoms used in HF patients include the Memorial Symptom Assessment Scale (MSAS) (18), modified for HF (19), and the Edmonton Symptom Assessment Scale (ESAS) (20). The MSAS-HF is a 32-item tool that rates frequency over the previous 2 weeks of symptoms, as well as their severity and distress, but its complexity and length may limit clinical use. The ESAS, which rates severity of 9 symptoms using a visual analog scale (a 100-mm line anchored by labels at the 0 [none] to 10 [worst possible] marked by the patient to indicate their status), has been administered to advanced HF patients (21), or modified as a 4-point scale (labeled not present, mild, moderate, and severe) administered to older patients with HF (22). In rating symptom severity, patients discriminate better with a 5-point numerical scale than a 10-point scale (23). For clinical use, the ESAS or a rating of common symptoms on a 5-point scale are appropriate to assess symptoms throughout the course of illness. A clinical interview should identify factors that precipitate, worsen, or improve each symptom, and in the case of pain, its location and character.

Clinical research should include patient reports of symptom frequency, severity, and interference in activity or distress caused by the symptom, in relation to the intervention studied. A working group of trial cardiologists recommends a “provocative dyspnea assessment” using a 5-item scale at multiple levels of activity to give a “dyspnea severity scale” from 1 to 25, although this is not tested or validated (24).

The majority of trials of therapies in HF have not evaluated symptoms as outcomes. Three research tools measuring HF-related quality of life, the Minnesota Living With Heart Failure (MLWHF) questionnaire (25), the Chronic Heart Failure (CHQ) questionnaire (26), and the Kansas City Cardiomyopathy Questionnaire (KCCQ) (27), are sensitive to changes in clinical status. All 3 tools ask the patients to rate how their HF has affected activities and the MLWHF and CHQ ask how HF impacts symptoms; thus, they are limited by the patient’s interpretation that a symptom or problem relates to HF. The KCCQ asks fatigue, shortness of breath, and swelling frequency, and amount they bothered over 2 weeks. A single-center study of persons with advanced HF found a correlation between the ESAS combined “symptom distress score” and KCCQ physical symptom score (24).

Palliation of symptoms. The pathophysiologic basis for HF-related fatigue, dyspnea, and compromised exertion argues for the use of treatments that block or modify the neurohormonal and cytokine abnormalities of HF to palliate symptoms. Many pharmacologic and device studies have documented improvement in NYHA functional classification and/or HF-related quality of life along with improvements in neurohormonal activation with the intervention. Few studies specifically assessed change in patient symp-

toms, rather than NYHA functional classification or HF-related quality of life.

In addition to therapies targeting the neurohormonal alterations in HF, other interventions have been documented to provide specific benefits. Many interventions commonly employed in palliative care have not been tested specifically in HF, but merit consideration by clinicians caring for HF patients.

Interventions to address the neurohormonal alterations in HF and symptoms. Angiotensin-converting enzyme inhibitors as a drug class improve HF patient duration of exercise (28), and presumably also as a class, improve HF symptoms. An early double-blind randomized trial of captopril demonstrated statistically significant improvement in patient rating of dyspnea, fatigue, orthopnea, and edema versus placebo in patients with NYHA functional class II to III HF (29). In this study, just under two-thirds of subjects improved with captopril, however, and one-third were unchanged. All angiotensin-converting enzyme inhibitors can be expected to improve symptoms in patients with LVSD. Studies in patients with HF_nEF are limited, but perindopril in elderly HF_nEF patients resulted in a statistically significant improvement in NYHA functional class and 6-min walk distance (30). A secondary analysis of Val-HeFT (Valsartan Heart Failure Trial) data demonstrated that valsartan improved composite fatigue and dyspnea scores versus placebo in patients with LVSD (31). Data about other angiotensin receptor blockers and symptoms are otherwise not available.

Beta-blockers as a class have variable impact on HF symptoms and overall quality of life (32), possibly relating to their adrenergic blocking profiles. A small randomized trial of carvedilol in advanced HF patients documented significant improvement in a 7-point symptom scale versus placebo (33), and a multicenter randomized controlled trial documented marked (21.1% vs. 16.1%) or moderate (28.5% vs. 23.9%) improvement in a global score for carvedilol versus placebo (34).

Whereas the RALES (Randomized Aldactone Evaluation Study) trial demonstrated statistically significant improvement in NYHA functional class with spironolactone in patients with advanced LVSD HF, only 41% of those receiving spironolactone improved, and 38% of them worsened (35). These modest results and absence of data about specific symptoms suggest that a cautious trial of aldosterone blockade is warranted with monitoring of patient-reported symptoms to assess individual benefit. Aldosterone blockade may help manage volume overload in addition to its neuroendocrine action. Serum potassium levels must be monitored when spironolactone is initiated. Investigation of spironolactone in HF_nEF is in progress.

All HF patients should be screened for sleep-disordered breathing in light of the over 50% prevalence in HF patients and the impact of sleep-disordered breathing on symptoms and right and left ventricular function (36). Continuous positive airway pressure (CPAP) reverses the adverse neu-

rohormonal activation for patients with sleep apnea and with Cheynes-Stokes (or periodic breathing) respiration (37). CPAP improves emotional function, fatigue, sense of control or mastery, social function, and vitality in patients with LVSD and sleep apnea (38). Heart failure patients with periodic breathing have improved quality of life with nocturnal oxygen supplementation (39). Sleep-disordered breathing treatment with CPAP or oxygen supplementation is warranted to improve symptoms at all phases of HF care, despite debate about the impact about these treatments on longevity.

Other treatments to palliate symptoms. Loop diuretics prescribed for volume overload in HF improve exertion and breathlessness (40), but activate the renin-angiotensin-aldosterone system, so they potentially exacerbate HF pathophysiology (41). Early in HF treatment and at points of decompensation, aggressive diuresis in patients with LVSD results in decreased patient reported dyspnea and improved global status (42). Diuretics to achieve and maintain euvolemia are considered important to symptom management throughout the course of both LVSD and HFnEF. The clinical assessment of volume status is a key skill for clinicians at all phases of HF care, including the end of life. B-type natriuretic peptide measurement is controversial but may help identify volume overload. Patients, families, and clinicians should routinely use weight as a proxy for volume, adjusting diuretics to maintain a euvolemic target weight.

Dietary intervention that specifically restricts fluids and sodium intake reduces fatigue and edema (43). Education for patients about HF and their management of sodium, exercise, and medications must be repeated and reinforced throughout the course of care for HF patients (44), especially at times of exacerbation. At all phases of HF care, patients and families should understand management of dietary sodium and fluid status as a means to improve symptoms. In addition, restricting fluid and sodium intake may reduce the need for diuretics and associated urinary urgency.

Oral nitrates are commonly prescribed to HF patients, although their impact on specific symptoms is not known. No evidence supports the use of oral nitrates to relieve dyspnea, but intravenous nitroglycerine relieved dyspnea in a randomized controlled trial for decompensated HF (45). Particularly when ischemia or overt volume overload are suspected, trial of oral or transdermal nitrates in an individual patient may be warranted.

In small randomized controlled studies, oral opioids improve dyspnea acutely and chronically in NYHA functional class II to IV patients, without significant adverse consequences. Opioids improve the ventilatory response to exercise (46–48). Several mechanisms may be important in the effect of opioids on dyspnea: they variably cause vasodilation, act on opioid receptors in the brain and in the lung to alter the perception of dyspnea, and are anxiolytic. Dihydrocodeine alters arterial chemosensitivity to oxygen and carbon dioxide in exercising HF patients. Opioids are appropriate for

the relief of dyspnea at all phases of HF care. Other interventions that impact chemosensitivity, such as caffeine, improve exercise endurance (49), so they may have a role in treatment of exertional dyspnea or fatigue.

Patients with HF and depression report more fatigue and other symptoms than those without depression (50). The evidence base to direct choice of antidepressants is weak; however, patients with renal impairment treated with selective serotonin reuptake inhibitors (SSRIs) are at risk for hyponatremia or fluid retention, likely due to increased antidiuretic hormone, so serum sodium must be carefully monitored (51). Tricyclic antidepressants (nortriptylene or desipramine) are appropriate alternatives to SSRIs, but have a quinidine-like effect on conduction, and at high doses can prolong QT intervals. Both SSRIs and tricyclic antidepressants require 2 weeks or longer to titrate. Methylphenidate and other psychostimulants have minimal adverse effects and have been used effectively in the elderly and in other chronic life-limiting illnesses for treatment of depression or fatigue. Benefit from psychostimulants is seen in 1 to 2 days.

Anxiety has not been well evaluated in HF; however, engaging spouses and increasing spousal sense of control improves HF patient emotional distress (52). Patients with better self-assessed control over their HF have less emotional distress as well as better exertional performance (53). A prospective cohort study combining a “mindfulness” support group and HF education resulted in statistically significant improvement in depression and anxiety scores (54). Benzodiazepines (such as lorazepam, which has no active metabolites and a 4 to 6 h length of action) are appropriate for treatment of distressing anxiety at any point in HF care.

Several studies demonstrate the benefit of exercise to endurance and quality of life in HF patients (55,56). Inspiratory respiratory muscle training improves blood flow to resting and exercising skeletal muscles, and improves exercise performance and dyspnea in HF patients (57–59). Specific thigh muscle training improves dyspnea as well as muscle strength (60), and should be the cornerstone of HF exercise programs. In a single-center trial, aerobic exercise improved the apnea-hypopnea index in patients with LVSD and sleep-disordered breathing (61). In HF patients with anemia, erythropoietin enhances exercise capacity (62).

Although pain is common in HF patients, its etiology and appropriate treatment remain to be elucidated (63). Chest pain is common, as is pain in other sites, with leg and joint pain predominating (64). Nonsteroidal anti-inflammatory drugs are contraindicated in HF patients because these drugs impact kidney function, cause sodium and fluid retention, and worsen HF (65–67). Osteoarthritis or chronic musculoskeletal pain can be treated with a combination of muscle-strengthening exercises, assistive devices, modalities (heat, cold, ultrasound), intra-articular joint injection, and opioids.

Opioids have diverse effects in the cardiovascular system, as well as the nervous and endocrine systems

Table 2 Elements of Communication About Prognosis With Heart Failure Patients and Families

"Bad news" conversation	Plan the delivery of sad or unexpected information, and warn the patient that you have bad news; follow the points below.
Ask-Tell-Ask	Ask what the patient understands (before you talk). Correct misunderstanding and Tell your information. Ask what questions they have, clarify information.
Simple, honest language	Define medical terms. Speak plainly and avoid euphemisms and relative statistics or percentages. Use numbers ("1 out of 5 people. . .").
Simple statistics	
Ground data in more than 1 way	Describe both chance of death and chance of life.
Hope for best, plan for the worst	Ask what the patient hopes for, and identify what you can also hope for.
"Both-And"	Plan for death or other bad outcomes "If things do not go as we hope." Create a dichotomy and address both issues.
Normalize uncertainty	Acknowledge that we can't know for sure, "like many things in life."
Partner and plan	Tell the patient you (or your team) will work <i>with</i> them to meet specific goals.
Deliver length of life in broad range	Provide a broad range "months to years," and allow for error on either end.
Empathize	Name your emotions ("I feel sad"), and identify emotions the patient expresses or might reasonably have ("you look surprised," "many would feel angry").
Follow-up	Summarize the plan and set an appointment to follow-up on plans and their status.

(such as regulation of vasopressin). Opioids can be safely administered to HF patients in cardiac anesthesia, although these drugs variably cause bradycardia, hypotension, and suppression of respiratory drive, so these effects should be monitored with parenteral administration.

General principles of opioid prescription are to: 1) begin therapy with short-acting opioids and titrate to the amount of pain relief desired by the patient; 2) treat intermittent pain with intermittent medication, and chronic or persistent pain with around-the-clock or long-acting opioids; and 3) accompany all opioid prescriptions with a stimulant laxative prescription. Morphine, codeine (and possibly hydromorphone) have active renally cleared metabolites that cause delirium and myoclonus, and are therefore appropriate only for intermittent use in HF patients. Fentanyl and methadone do not have active metabolites; however, each has unique issues. Fentanyl is approved only for use in opioid-tolerant patients in either oral-buccal mucosal or transdermal delivery systems. Methadone accumulates in tissues, and the dose and interval must be titrated for 5 to 7 days when it reaches a steady state. Methadone can variably prolong rate-corrected QT interval and rarely cause torsades de pointes (usually at doses >100 mg/day), so electrocardiograms should be evaluated at baseline and 30 days after initiation of methadone (68).

In patients with reduced systolic function, inotrope therapy may improve quality of life, despite increased risk of sudden death (69,70). Cardiac resynchronization therapy (71) and destination left ventricular assist devices (72) improve exertion and HF-related quality of life for select patients, although data about their impact on specific symptoms are not available.

Communication with patients about dying and approach to care. Although the focus of therapy for many patients is to improve function and defer death, the life-limiting nature of HF and increased risk of sudden cardiac death (SCD) with HF should be acknowledged at the time of HF diagnosis as part of HF patient/family education

(73). Providing HF patients and families a warning that death may come suddenly or with chronic illness helps remove surprise from later communication when the patient deteriorates or at the end of life (74). Knowledge of the life-limiting nature of HF may also help patients and their families "fight" HF by diet, exercise, and medications, in addition to helping them "plan for the worst" should they die sooner than preferred. The subject of dying need be only reviewed when the patient inquires, it is required for decision making about interventions, or with a decline in status. Physicians and nurses should be prepared to discuss dying and prognosis whenever they arise. Answers about prognosis, should be honest, and uncertainty should be acknowledged. Discussions with HF patients about length of life should give a range of time, and should acknowledge the possibility for error at either end.

All HF patients and their families should have a plan to manage potential SCD, including in selected LVSD patients once HF therapy has been optimized, potentially life-prolonging interventions such as implantable cardioverter defibrillators. Basic approaches to giving bad news, participatory decision making, and communicating about the end of life should be learned by all clinicians caring for HF patients. These are presented in detail in another review (71), but key aspects are outlined in Table 2. Training in these specialized communication skills integrated into oncology fellowships and continuing education (75), should serve as a model for cardiology.

Preferences for approach to care in advanced disease may be more related to educational level and health literacy or the length of discussions than to race or ethnic background. Allowing for discussions over time or using tools such as videos reduces disparities (76). The Ask-Tell-Ask framework is particularly important when caring for patients of different ethnic or racial groups from one's own. Patients who prefer to not participate in

decision making should be asked to appoint someone to make decisions on their behalf.

End-of-Life Care for HF Patients

The “end of life” for a given HF patient is not easily predicted by clinical data or symptoms. Nurses’ predictions of death for hospitalized HF patients in a large multicenter trial were better than a prognostic model (incorporating blood urea nitrogen, systolic blood pressure, and 6-min walk score) (77). In a community study, symptom prevalence did not distinguish NYHA functional class III to IV patients who died from those who survived 1 to 2 years (78). Risk models may identify patients at high likelihood of death in 6 to 12 months, although these models have not been prospectively tested (79,80). In a single center, HF patients did not perceive the life-limiting nature of HF (81). In combination, these barriers support providing palliative care to all HF patients, and acknowledging HF as a life-limiting illness, even when working toward patient and family goals to prolong life.

The course to death in patients should not be characterized by severe dyspnea or volume overload. Rather, most dying patients managed by HF specialists experience metabolic derangement and coma, or sudden death (82,83), not congestion and dyspnea. Heart failure patients make decisions about treatments based on a description of what their course might be and mode of death, in addition to likely benefits and burdens (84,85). In time tradeoff or treatment tradeoff studies, patient decisions are not necessarily related to their HF status or symptom severity (86,88), and often change over time (87). How these hypothetical choices relate to real-life decisions is not known.

Physicians lack experience in discussing decisions such as deactivation of implanted defibrillators at the end of life (88), yet patients experiencing 5 or more shocks have poor quality of life (89), and may want an option to deactivate the device. Advanced HF patients who prefer to be allowed to die naturally when the time comes should have a defibrillator electively deactivated. Any center that implants defibrillators should have a clearly defined process for their deactivation. A decision to discontinue or forego a treatment such as defibrillation is ethically and legally equivalent to a decision to initiate a treatment (90), and follows the same informed decision-making process. Clinicians caring for HF patients must acquire the skills to make decisions about care based on the patient’s preferences and the likely benefit and burden of therapies for that individual.

Management at the end of life. Advanced HF should provoke a re-evaluation of medications, dietary sodium consumption, and interventions that might improve the patient’s status (91). At a shift in focus of care, such as the end of life, clinicians ought to re-evaluate all treatments relative to the goals of care, and discontinue therapies that are burdensome or that do not provide symptomatic relief. Because medications and treatments that address the neurohormonal and sympathetic disarray in HF improve symp-

toms, these should be continued to the extent that blood pressure and function tolerate. No studies have evaluated the impact of dose reduction on symptoms. In a single center, in significantly volume-overloaded patients with advanced HF, carvedilol initiation and up-titration was better tolerated and associated with lower rates of death, hospitalization, or study drug withdrawal, than placebo (92). Until data about symptoms and well-being are available about HF medications at the end of life, clinicians will need to decide about medication continuation with individual patients and families based on their individual goals of care.

Studies of palliative care programs that included HF patients have not characterized either the patients’ HF status or use of evidence-based medications, but the programs improved dyspnea, anxiety, and spiritual well-being (93), caregiver satisfaction, and increased rates of death at home (94). When HF clinicians identify patients’ or families’ worries, fears, and spiritual and existential issues, the clinicians may create a “virtual team” using resources from the community and other clinicians to provide interdisciplinary support.

Bereavement support, for losses in function and social roles throughout HF and at the end of life in anticipation of death, is an area where additional research is needed. Similarly, support for spiritual and existential issues in HF will benefit from more investigation. Clinicians should inquire about and acknowledge concerns, and identify resources to support the patient and family. Throughout care, maintaining contact, even by brief notes or telephone, is valued by patients and families. After death, a note or telephone call from clinicians to the family to express condolences is important to the family and as closure for the clinician (74).

Hospice care for HF patients. Reimbursement models emphasize a false dichotomy in which hospice or formal palliative care is expected to begin and HF care cease at some difficult-to-identify point. In a secondary analysis of patients hospitalized with acutely decompensated HF, rates of discharge from hospitals to hospice were very low, although they varied by geographic region (95). Patients discharged to hospice in this study were remarkably similar to those who died in the hospital, except that patients who died had significantly more invasive procedures than those sent to hospice.

Hospice care for HF patients varies among agencies: hospices generally provide oral medications for HF and opioids for symptom management, but few hospices, generally those with large patient censuses, provide more complex and expensive treatments such as intravenous medications or inotropes (96). Hospice nurses lack knowledge and self-assessed competency about HF management (97). Good end-of-life care for HF patients will require clinicians with HF expertise to work directly with hospice staff to collaboratively manage care and to improve hospice staff knowledge and skills regarding HF.

Once enrolled in the Medicare hospice benefit, the length of care is not limited; however, at the end of specified periods, hospices must discharge the patient or recertify him or her as likely to die within 6 months. Prognostic tools may be helpful in patient re-evaluation, particularly when, with careful management, the patient's status has improved. Patients may elect to revoke the hospice benefit at any time because they desire a different approach to care. When hospice care ceases for either reason, it is appropriate to re-evaluate the patient's status and preferences and reclarify goals for care. A palliative focus often remains appropriate.

Conclusions

Comprehensive HF care should integrate palliative care throughout the course of management. The etiology of many HF symptoms relates to neurohormonal and cytokine activation, and the resulting impact on skeletal and respiratory muscles. Interventions to palliative symptoms include evidence-based therapies for the neurohormonal derangement in HF, but data about therapies that specifically improve symptoms are sparse. Evidence supports some other interventions, including specific exercise and opioids for dyspnea, but additional data are needed to inform treatment of depression, anxiety, pain, and spiritual distress, among other problems, in HF patients and their families.

Data regarding symptom relief should be included in clinical trials for HF, and specifically to understand palliative therapies in advanced HF. Palliative care for HF should incorporate evidence-based HF therapies and interdisciplinary interventions to address multiple domains of patient and family distress.

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